

Claim Amendments

Please amend the claims as follows:

Cancel claims 1-68 without prejudice or admission, and add new claims 69 – 117

as follows:

1. (Canceled herewith)
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69. (New) An antibody that is capable of binding human CTLA4, which antibody comprises a heavy chain variable region having a contiguous amino acid sequence encoded by a human V_H 3-30.3 or V_H 3-33 gene, said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6.

70. (New) An antibody according to claim 69, wherein said antibody binds human CTLA4 with a binding affinity of about 10⁹ M⁻¹ or greater.

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71. (New) An antibody according to claim 69, wherein said antibody does not bind CTLA4 from mouse.

h

72. (New) An antibody according to claim 69, wherein said antibody binds CTLA4 from cynomolgus monkey.

73. (New) An antibody according to claim 69, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about 1 µg/mL.

74. (New) An antibody according to claim 69, which antibody reduces binding of human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least about 1 µg/mL.

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75. (New) An antibody according to claim 69 wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39.

76. (New) An antibody according to claim 69, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

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77. (New) An antibody according to claim 69, which antibody further comprises a light chain variable region having a contiguous amino acid sequence encoded by a human V_K A-27 or V_K L-15 gene, said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5.

78. (New) An antibody according to claim 77, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36.

79. (New) An antibody according to claim 77, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

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80. (New) An antibody that is capable of binding human CTLA4, which antibody comprises a light chain variable region having a contiguous amino acid sequence encoded by a human V_K A-27 or V_K L-15 gene, said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5.

81. (New) An antibody according to claim 80, wherein said antibody binds human CTLA4 with a binding affinity of about $10^9 M^{-1}$ or greater.

82. (New) An antibody according to claim 80, wherein said antibody does not bind CTLA4 from mouse.

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83. (New) An antibody according to claim 80, wherein said antibody binds CTLA4 from cynomolgus monkey.

84. (New) An antibody according to claim 80, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about $1 \mu g/mL$.

85. (New) An antibody according to claim 80, which antibody reduces binding of human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least about $1 \mu g/mL$.

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86. (New) An antibody according to claim 80, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36.

87. (New) An antibody according to claim 80, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

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88. (New) An antibody according to claim 80, which antibody further comprises a heavy chain variable region having a contiguous amino acid sequence encoded by a human V_H 3-30.3 or V_H 3-33 gene, said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6.

89. (New) An antibody according to claim 88, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39.

90. (New) An antibody according to claim 88, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

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91. (New) A human antibody that binds human CTLA4 with a binding affinity of about 10^9 M^{-1} or greater.

92. (New) An antibody according to claim 91 that does not bind CTLA4 from mouse.

93. (New) An antibody according to claim 91, wherein said antibody binds CTLA4 from cynomolgus monkey.

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94. (New) An antibody according to claim 91, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about $1 \mu\text{g/mL}$.

95. (New) An antibody according to claim 91, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about $1 \mu\text{g/mL}$.

96. (New) An antibody according to claim 91, which antibody comprises a heavy chain variable region having a contiguous amino acid sequence encoded by a human V_H 3-30.3 or V_H 3-33 gene, said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6.

97. (New) An antibody according to claim 96, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39.

98. (New) An antibody according to claim 96, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

99. (New) An antibody according to claim 96, which antibody further comprises a light chain variable region having a contiguous amino acid sequence encoded by a human V_K A-27 or V_K L-15 gene, said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5.

100. (New) An antibody according to claim 99, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36.

101. (New) An antibody according to claim 99, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

102. (New) An antibody according to claim 91, which antibody comprises a light chain variable region having a contiguous amino acid sequence encoded by a human V_K A-27 or V_K L-15 gene, said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5.

103. (New) An antibody according to claim 102, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36.

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104. (New) An antibody according to claim 102, wherein the contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

105. (New) An antibody according to claim 102, which antibody further comprises a heavy chain variable region having a contiguous amino acid sequence encoded by a human V_H 3-30.3 or V_H 3-33 gene, said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6.

106. (New) An antibody according to claim 105, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises at least one CDR amino acid sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39.

107. (New) An antibody according to claim 105, wherein the contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

108. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:16; and
- (b) a light chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:6,

wherein said stringent conditions comprise hybridization in buffer comprising 5 x SSC and 0.1% SDS at 65 °C with a wash of 0.2 x SSC and 0.1% SDS at 65 °C, and wherein said antibody is capable of binding to CTLA4.

109. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:18; and
- (b) a light chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:8,

wherein said stringent conditions comprise hybridization in buffer comprising 5 x SSC and 0.1% SDS at 65 °C with a wash of 0.2 x SSC and 0.1% SDS at 65 °C, and wherein said antibody is capable of binding to CTLA4.

110. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:22; and
- (b) a light chain variable amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions to the complement of SEQ ID NO:12,

wherein said stringent conditions comprise hybridization in buffer comprising 5 x SSC and 0.1% SDS at 65 °C with a wash of 0.2 x SSC and 0.1% SDS at 65 °C, and wherein said antibody is capable of binding to CTLA4.

111. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:17; and
- (b) a light chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:7,

wherein said antibody is capable of binding to CTLA4.

112. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:19; and
- (b) a light chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:9,

wherein said antibody is capable of binding to CTLA4.

113. (New) A human antibody comprising:

- (a) a heavy chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:23; and
- (b) a light chain variable amino acid sequence having at least 80% amino acid residue identity with the amino acid sequence set forth in SEQ ID NO:13,

wherein said antibody is capable of binding to CTLA4.

114. (New) An antibody selected from the group consisting of 10D1, 4B6 and 11E2.

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115. (New) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:19; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:9.

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116. (New) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:17; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:7.

117. (New) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:23; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:13.